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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,825	08/25/2003	Jonathan Lee Vennerstrom	0685-UNMC-63183	2919

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DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER

ZUCKER, PAUL A

ART UNIT PAPER NUMBER

1621

DATE MAILED: 07/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/647,825

Applicant(s)

VENNERSTROM, JONATHAN LEE

Examiner

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/23/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: Page 5, line 1:
The heading "Brief Descriptions of the Drawing" should be changed to "Brief Description of the Drawings". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "at a temperature between about 35°C and about 50°C" in lines 6-7. It is unclear whether this temperature range applies to the reaction mixture, the generation of the acid catalyst or both. Claim 1 and its dependents are therefore rendered indefinite.
3. Claims 3 -9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 recites the limitations "said lower alcohol comprises ethanol" in line 2 and "said acyl halide comprises acetyl chloride" in lines 2-3. Claim 1 recites the limitation "a lower alcohol" in lines 1-2. Claim 2 upon which claim 3 depends recites the limitation "an acyl halide" in line 2. It is therefore unclear whether Applicants contemplate single compounds or compositions containing an

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alcohol and acyl halide. Claim 3 and its dependents are therefore rendered indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
4. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dox et al (Journal of Biological Chemistry, Esterification of Creatine, 1992, 54 pages 671-673) in view of Nudelman et al (Synthetic Communications, Acetyl Chloride – Methanol as a Convenient Reagent for: a) Quantitative Formation of Amine Hydrochlorides b) Carboxylate Ester Formation c) Mild Removal of N-t-BOC-Protective Group, 1998, 28, pages 471-474).

Instantly claimed is a process for the esterification of creatine employing an acid catalyst that is generated *in situ*. Steps for purification of the final product are claimed as well.

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Dox teaches (Page 672, lines 23-36) a process for the formation of creatine ethyl ester hydrochloride. Creatine in absolute ethanol (ratio 1g :10 ml) is saturated with dry HCl gas (presumably with heating due to dissolution of HCl). The ethyl ester crystallized as it formed and was recrystallized from ethanol (presumably with filtration, drying and recovery). It is obvious to use the least amount of solvent necessary since the product crystallizes out of solution and use of the minimum amount of solvent would maximize product recovery. Dox teaches (Page 672, lines 4-5) the use of cooling (ice water ~6 °C) in crystallization as well.

The difference between the process taught by Dox and that instantly claimed is that the acid catalyst instantly employed is generated *in situ* while that employed by Dox has exogenous origins.

Nudelman, however, teaches a method for the esterification of carboxylic acids to give the corresponding esters (Page 474, lines 7-17) using HCl in alcohol (methanol or ethanol) generated by the addition of acetyl chloride to the alcohol solution in equivalent or excess amount. Nudelman teaches (Page 474, lines 12 –14) that addition of acetyl chloride to the alcohol solution is exothermic and therefore results in heating of the reaction mixture. The use of between 1 and 2 equivalents in the instant case is obvious since the product ester itself consumes 1 equivalent of HCl and less than 2 equivalents are required since HCl acts as a catalyst. The Examiner notes that the generation of HCl by this method produces ethyl acetate as a by-product and thus the use of the less expensive denatured alcohol instead of

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absolute is obvious. The Examiner further notes that the reaction times, reactant and substrate-catalyst ratios and temperature ranges are parameters that one of ordinary skill in the art would routinely adjust in the optimization of a process. Therefore, in the absence of unexpected results, limitations with respect to these variables cannot confer patentability on an otherwise obvious process.

The motivation to modify the method for introducing HCl in the process of Dox using the method of Nudelman comes from Nudelman who teaches that the use of HCl gas produces corrosion and exposure to the corrosive HCl which can be avoided by the use of his method. There would have been a reasonable expectation for success based on the fact that Nudelman teaches that his method is suitable for carrying out esterifications,

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art.

Conclusion

5. Claims 1-17 are pending. Claims 1-17 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 571-272-0650. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone

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number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Paul A. Zucker', is written over a horizontal line.

Paul A. Zucker, Ph. D.
Patent Examiner
Technology Center 1600